UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,123	02/12/2002	Jing Li	006539.00046	2334

22907 7590 02/10/2006

BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

EXAMINER	
O FARRELL, THOMAS JOHN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,123	LI ET AL.	
	Examiner	Art Unit	
	Thomas J. O'Farrell	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 39-56* is/are pending in the application.

4a) Of the above claim(s) *4-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 39-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-3 and 39-56 are pending in the instant application. Claims 4-38 were withdrawn from consideration as being drawn to a nonelected invention. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections are either newly applied as necessitated by amendment or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Applicant's arguments, see page 12, filed 11/18/2005, with respect to the rejection of claims 1-3 under 35 USC §112, second paragraph, have been fully considered and are persuasive. The previous rejection of claims 1-3 under 35 USC §112, second paragraph based on the preamble not agreeing with the final step of the method regarding the intent of the method to diagnose a cancer only or to diagnose a precancerous lesion as well, has been withdrawn as the amended claim 1 now recites ""…..indicates the presence of a precancerous lesion or cancer in the mammal".

New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. Claims 1-3 and 39-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing breast cancer in a human, comprising detecting and measuring a human WIP1 gene, having the nucleotide sequence of SEQ ID NO:1 or 3, copy number in human breast tissue that is suspected to be cancerous, thereby generating data for a test gene copy number; and comparing the test gene copy number to data for a control gene copy number, wherein about a 2.5 fold or greater amplification of the gene in the human breast tissue relative to the control indicates the presence of breast cancer in the human, does not reasonably provide enablement for diagnosing *any* cancer in *any* mammal by measuring and detecting *any* amplification in the gene copy number of a WIP1 gene having a nucleotide sequence homology of at least 70, 90, or 95% sequence identity to SEQ ID NO:1 or 3 or *a* sequence of SEQ ID NO: 1 or 3 in *any* biological sample that is suspected to be precancerous or cancerous. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These

factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

The claims are broadly drawn to a method of diagnosing *any* precancerous lesion or *any* cancer in *any* mammal by detecting and measuring the gene copy number of a WIP1 gene having a nucleotide sequence homology of at least 70, 90 or 95% sequence identity to SEQ ID NO:1 or 3 or where the WIP1 gene has *a* nucleotide sequence of SEQ ID NO:1 or 3 in *any* biological sample from a region of the mammal that is suspected to be precancerous or cancerous, thereby generating data for a test gene copy number; and comparing the test gene copy number to data for a control gene copy number, wherein *any* amplification of the gene in the biological sample relative to the control indicates the presence of a precancerous lesion or a cancer in the mammal. The claims are also broadly drawn to the above method of diagnosing *any* cancer wherein the biological sample is selected from the group consisting of breast tissue, lung tissue, prostate tissue, ovarian tissue, and colon tissue.

The amount of direction or guidance:

The specification teaches that the detection of amplified or overexpressed oncogenes is an important method for diagnosing cancer (page 4). The specification also teaches that WIP1 is a serine/threonine specific protein phosphatase type 2C (PP2C) family member whose expression is induced in response to gamma or UV radiation in a p53-dependent manner (pages 37 and 38). The specification broadly defines the WIP1 gene as WIP1 nucleic acids (DNA or RNA) that can include their polymorphic variants, alleles, mutants, and interspecies homologs that have substantial nucleotide sequence homology with the nucleotide sequence of the GenBank entry AAB61637 or SEQ ID NO:1 (pages 21 and 22). The specification also teaches that expression of WIP1 can transform normal cells into cells with a more cancerous phenotype (page 39). The specification also teaches that WIP1 is found within human chromosome 17q23, which is one of the most frequently amplified regions in human breast cancer (page 39). The specification teaches that the WIP1 gene is amplified and/or overexpressed in several breast tumor cell lines (Table 1). The specification also teaches that the WIP1 gene is overexpressed in several primary tumor samples of different types of cancer and amplified in several primary breast tumor samples (Table 2). The specification further teaches methods for detecting and quantitating WIP1 gene amplification and level of expression (pages 40-45).

Presence and absence of working examples:

The specification teaches that the WIP1 gene is amplified and/or overexpressed in several cell lines derived from human breast cancer tumors (Table 1). With regard to

gene amplification in primary tumors, the specification teaches that the WIP1 gene is amplified in 16% of a sampling of human breast tumors and 3% of a sampling of human lung tumors, where an amplification of 2.5 fold or greater compared to the control is considered to be amplified (Table 2 and page 40). The specification further teaches that amplification of the WIP1 gene was not found in human colon, prostate, and ovarian tumors (Table 2) and the specification is silent with respect to the amplification of the WIP1 gene in numerous other types of cancers that exist such as brain and liver cancer. The specification teaches that WIP1 was overexpressed in 8-47% of the tumors selected from breast, colon, lung, metastatic prostate, and ovary tissues and was not found overexpressed in primary prostate tumors (Table 2). The specification teaches that while WIP1 was overexpressed in 47% of the metastatic prostate tumors examined, the genomic gene itself was not found amplified in any metastatic prostate tumors (Table 2). Therefore, the teachings of the specification do not address an association of the amplification of the WIP1 gene with *any* type of cancer and the teachings with regard to the amplification of the WIP1 gene in colon, prostate, lung, and ovarian tumors indicate, in fact, that there is not an association of the amplification of the WIP1 gene with *any* type of cancer. In addition, the specification teaches that there is no predictable correlation between WIP1 overexpression and genomic gene amplification. The specification is also silent with regards to an association of the amplification of the WIP1 gene with any precancerous tissues. The specification is also silent with regard to the ability to diagnose *any type* of cancer, brain cancer for example, based on amplification of the WIP1 gene in a particular tissue, breast tissue for example

(instant claim 2). Also, the specification only teaches WIP1 gene amplification in human cancer samples and therefore is also silent with regard to the ability to diagnose *any* mammal with cancer by detecting and measuring a WIP1 gene copy number. The specification is also silent with regard to the amplification of *any* WIP1 gene with 70-99% sequence identity to SEQ ID NO:1 or 3, such as variants and homologs, being diagnostic of cancer. It is noted that the studies disclosed in the specification only involve the human WIP1 gene (SEQ ID NO:1) (pages 39-41 and Tables 1 and 2), however, Fiscella et al. teach that other protein phosphatase type 2C family members exist that have substantial amino acid homology to WIP1 (see Fiscella, et al., (1997), *Proc. Nat. Acad. Sci.*, vol. 94, see Fig. 1). Therefore, from the limited amount of guidance and working examples disclosed in the specification, the skilled artisan would not be able to predictably diagnose *any* precancerous lesion or *any* cancer in *any* mammal by measuring and detecting *any* amplification in the gene copy number of *any* WIP1 gene or homologue in *any* biological sample that is suspected to be precancerous or cancerous.

The state of the prior art and the predictability or unpredictability of the art:

Several studies have examined the association of amplification and overexpression of the WIP1 gene with different types of cancer. These studies reveal that the art is unpredictable with regard to an association of the amplification of the WIP1 gene with various types of cancer. Kansai et al. teach that Wip1 is not expressed at higher levels in human stomach, colorectal, or heptacellular cancers compared to

corresponding non-cancerous tissues, suggesting that the WIP1 genomic gene is not amplified in these cancers (see Kanai, et. al., (2001), *J. Cancer Res. Clin. Oncol.*, vol. 127, Table 3). In addition, Bulavin et al. teach that *PPM1D* (WIP1) is amplified and overexpressed in human breast cancer cell lines BT-474 and MCF7 but not in other breast cancer cell lines NCI-ADR and MDA-N or in cell lines derived from kidney carcinomas (ACHN) or T-cell leukemias (Molt4) (see Bulavin, et. al., (2002), *Nat. Gen.*, vol. 31, Figure 4). Furthermore, with regard to an association of the amplification of homolog variants of the WIP1 gene with cancer, Lavi et al. teach that PP2Calpha was expressed at *lower* levels in 7 out of 8 colorectal tumors compared to adjacent normal colon tissues, suggesting that amplification of the PP2Calpha homolog of the WIP1 gene is not associated with colorectal cancer (see Lavi et al., WO 97/10796, page 46, lines 19-22). In addition, the art does not support a predictable correlation with regard to amplification of WIP1 gene homologs and cancer in mammals other than humans. Saadat et al. teach that the rat PP2Calpha homolog of the WIP1 gene was expressed at lower levels in all of the six *rat* hepatomas examined compared to normal rat liver cells, suggesting that the amplification of PP2Calpha homologs of the WIP1 gene is also not associated with cancer in non-human mammals (see Saadat et al., (1995), *Oncology Res.*, vol. 7, Figure 1). Furthermore, a WIP1 homolog with 96% sequence identity to SEQ ID NO:1 exists in Macaca fascicularis (see GenEmbl accession number AB168475.1 and result 11 of search of SEQ ID NO:1 in GenEmbl database) as well a homologue in mouse with 75% sequence identity to SEQ ID NO:1 (see GenEmbl accession number BC0234492.1, and result 15 of search of SEQ ID NO:1 in GenEmbl

database), however, the art is silent with respect to an association of the amplification of these genes with any cancers. Furthermore, the collective teachings of the specification and the art teach that the frequency of amplification of the WIP1 gene varies in different cancers, such as breast and ovarian cancers, and therefore the skilled artisan would not be expected to reproducibly diagnose a cancer in a particular tissue (such as ovarian cancer) by analyzing the amplification of the WIP1 gene in tissue from a disparate organ (such as the breast). Thus, the teachings in the art show that no predictable correlation can be made between the amplification in the gene copy number or transcript number of *any* WIP1 gene or homologue in *any* biological sample with *any* cancer in *any* mammal.

The level of skill in the art:

The level of skill in the art is deemed to be high.

The quantity of experimentation necessary:

Based on the limited guidance in the specification, and the unpredictability taught in the art, it would require undue experimentation for one of skill in the art to practice the invention as it is broadly claimed. The skilled artisan would have to test an association between the amplification of the WIP1 gene with cancer by testing an exhaustive list of different types of cancers, different biological samples (organ tissues), different precancerous tissues, different homologs (including interspecies homologs) and variants of WIP1 genes encompassed by the amended claims, and different species of mammals in the experimental system to be able to predictably diagnose *any* cancer in

any mammal by measuring and detecting amplification in the gene copy number of *any* WIP1 gene with 70-100% sequence identity to SEQ ID NO:1 or 3 in *any* biological subject suspected to be precancerous or cancerous. Based on the unpredictability in the art and the lack of guidance in the specification with regard to diagnosing *any* cancer in *any* mammal by measuring and detecting amplification in the gene copy number of *any* WIP1 gene with 70-100% sequence identity to SEQ ID NO:1 or 3 in *any* biological sample suspected to be precancerous or cancerous, it is clear that such experimentation would require an extremely large amount of unpredictable trial and error analysis. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the limited amount of working examples and the negative teachings of the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one skilled in the art to perform the methods of the instant claims as written.

Response to Arguments

5. The response traverses this rejection. The response asserts that enablement is not precluded by the necessity of some experimentation such as routine screening, even if it is extensive routine screening, or if the specification provides a reasonable amount of guidance (pages 7 and 8). The response asserts that guidance is provided in

the specification with regard to determining sequence identity and how to measure copy number (pages 8 and 9). This argument has been thoroughly reviewed but was not found persuasive. The guidance provided by the specification with regard to determining sequence identity and copy number is general. However, this guidance does not provide a predictable correlation between amplification of the claimed WIP1 sequences and *any* type of cancer. The skilled artisan would have to test an association of the amplification of the WIP1 gene and variants encompassed by the currently amended claims to representative amounts of different types of cancers, different biological samples (organ tissues), different precancerous tissues, and different species of mammals in the experimental system to be able to predictably diagnose *any* cancer in *any* mammal by measuring and detecting amplification in the gene copy number of *any* WIP1 gene with 70-100% sequence identity to SEQ ID NO:1 or 3 in *any* biological subject suspected to be precancerous or cancerous. This experimentation is extensive with many intervening steps not providing any guarantee of success in succeeding steps. In addition, as noted above in para 4, the specification and the art teach unpredictability with regard to an association of the amplification of the human WIP1 gene and its homologues, including those in other mammals, with various types of cancer. It is also noted that the specification teaches that sequence identity to the claimed sequences may be determined over a comparison window, however, the specification does not teach which sequences within the claimed sequences can be used for the comparison window. Therefore, the skilled artisan may find significant identity for a sequence in question with the claimed sequences for a small portion of the

total sequence, 70% or greater for example, while the rest of the sequences may have low identity resulting in the identification of a sequence encompassed by the claims that may be completely unrelated to WIP1. This would significantly add to the extensive trial and error analysis needed for the skilled artisan to practice the claimed invention. Extensive trial and error analysis that is not routine, further substantiated by unpredictability with regard to an association of the amplification of the human WIP1 gene and its encompassed homologues with various types of cancer taught by the specification and the art, would be required of the skilled artisan to practice the invention as broadly as it is claimed.

The response asserts that amplification of WIP1 in a representative amount of different tumors is taught in the specification (page 9). The response asserts that the teachings of Table 2 does not mean that the WIP1 gene is not amplified in colon, metastatic prostate or ovary tumors, only that amplification was not detected in this data set. The response asserts that WIP1 overexpression was detected in colon, metastatic prostate or ovary tumors. This argument has been thoroughly reviewed but was not found persuasive. The assertion that WIP1 may be found amplified in colon, metastatic prostate or ovary tumors in other data sets is speculation and provides no further predictability with regard to the amplification of WIP1 in *any* cancer. While it is noted that WIP1 was over expressed in some breast, colon, lung, metastatic prostate, and ovary tumors, the claims are broadly drawn to the measurement of WIP1 genomic gene copy number amplification and amplification of the WIP1 genomic gene was only seen in two of the six different tumor types. Furthermore, it is noted that while 47% of

metastatic prostate tumors sampled in the specification had overexpressed levels of WIP1, none of these tumors had WIP1 genomic gene amplification, indicating no predictable correlation between WIP1 overexpression and amplification of genomic gene copy number. Therefore, the examiner maintains that the specification does not teach a predictable association between amplification of the WIP1 genomic gene and a representative amount of different cancers.

For these reasons and the reasons already made of record, the rejection is maintained.

6. Claims 1-3 and 39-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods of diagnosing a precancerous lesion or a cancer in a mammal comprising detecting and measuring the WIP1 gene copy number in a biological sample suspected to be precancerous or cancerous. While the specification has taught methods of diagnosing a cancer in a human comprising detecting and measuring the human WIP1 gene copy number in a biological subject, the claims encompass methods of diagnosing a cancer in a mammal comprising detecting and measuring the gene copy number of a large genus of variant and homolog genes with 70-100% sequence identity to SEQ ID NO:1 or 3 or a WIP1 gene that has *a*,

interpreted as any part of, the nucleotide sequence of SEQ ID NO:1 or 3 in a biological sample which have not been taught or described in the specification. In addition, the specification teaches that sequence identity to the claimed sequences may be determined over a comparison window, however, the specification does not teach which sequences within the claimed sequences can be used for the comparison window. If small sequences within SEQ ID NO: 1 or 3 are used for the comparison window, the claims would further encompass genes having significant identity to SEQ ID NO:1 or 3 for a small portion of the total sequence, 70% or greater for example, while the rest of the sequence may have low identity, resulting in the identification of sequences that may be completely unrelated to WIP1. Based on the broad definition of WIP1 genes encompassed by sequences of 70-100% identity to SEQ ID NO: 1 or 3 and sequences comprising portions of SEQ ID NO:1 or 3, the large genus of WIP1 genes recited in the instant claims encompasses structurally and functionally distinct molecules, which have not been taught or described in the specification, whose amplification would not necessarily be expected to be associated with cancer. The specification provides no correlation between the structure of potential WIP1 homologs or portions of WIP1 and function either of encoded protein or functional association to cancer in general, or any particular type of cancer. The skilled artisan would have no way of knowing which of these genes to detect the amplification of for the purposes of diagnosing a cancer. In addition, the art does not support a predictable relationship between genes with homology to human WIP1 and gene copy number amplification in cancer. In fact, Lavi et al. teach that a homologous gene of the same family of phosphatases as WIP1,

protein phosphatase 2Calpha, which has regions of >70% sequence identity to human WIP1 (Fiscella et al., 1997, PNAS USA, vol. 94, pages 6048-6053, see page 6050, column 1, para 1, lines 11-15 of Fiscella), was expressed at *lower* levels in 7 out of 8 human colorectal tumors compared to adjacent normal colon tissues, suggesting that there is not an association of the amplification of certain genes with homology to human WIP1 and cancer (see Lavi et al., WO 97/10796, page 46, lines 19-22). The disclosure of SEQ ID NO: 1 and 3 is not representative of the broad variable genus of polynucleotides encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 1 or 3, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483,

claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Response to Arguments

7. The response traverses this rejection. The response asserts that the specification adequately describes the claimed methods and teaches the identity of a WIP1 gene having a nucleotide sequence homology of at least 70% identity to SEQ ID NO: 1 or 3 (page 11). This argument has been thoroughly reviewed but was not found persuasive. While the specification teaches the identity of a WIP1 gene having a nucleotide sequence homology of at least 70% identity to SEQ ID NO: 1 or 3, as noted above in para 6, the claims encompass methods of diagnosing a cancer in a mammal comprising detecting and measuring the gene copy number of a large genus of variant

and homolog genes with 70-100% sequence identity to SEQ ID NO:1 or 3 or a WIP1 gene that has *a*, interpreted as any part of, the nucleotide sequence of SEQ ID NO:1 or 3 in a biological sample which have not been taught or described in the specification. As noted above in para 6, based on the broad definition of WIP1 genes encompassed by the sequences of 70-100% identity, which includes sequences that may be completely unrelated to WIP1 based on the comparison window chosen for determining sequence identity, and sequences comprising portions of SEQ ID NO:1 or 3, the large genus of WIP1 genes recited in the instant claims encompasses structurally and functionally distinct molecules, which have not been taught or described in the specification, whose amplification would not necessarily be expected to be associated with cancer. Also, the specification provides no correlation between the structure of potential WIP1 homologs or portions of WIP1 and function either of encoded protein or functional association to cancer in general, or any particular type of cancer. In addition, as noted above in para 6, the art does not support a predictable relationship between genes with homology to human WIP1 and gene copy number amplification in cancer. The examiner maintains that the disclosure of SEQ ID NO: 1 and 3 is not representative of the broad variable genus of polynucleotides encompassed by the claims.

For these reasons and the reasons already made of record, the rejection is maintained.

Claim Rejections - 35 USC § 102

8. Claims 1-3 and 39-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Kallioniemi et al. (herein referred to as Kallioniemi, *Proc. Natl. Acad. Sci. USA*, vol. 91, pages 2156-2160, 03/1994), as defined by Wu et al. (herein referred to as Wu, *Cancer Res.*, vol. 61, pages 4951-4955, 07/2001).

Its is noted that the examiner interprets "...a nucleotide sequence of SEQ ID NO..." in claims 45-47 and 54-56 as any sequence within the recited sequences.

Wu teaches that the human WIP1 gene is located in the 17q22-23 region of chromosome 17 (see Figure 1 of Wu). Kallioniemi teach a method of detecting and measuring DNA sequence copy number increases for the 17q22-24 region in several human primary breast tumors and breast cancer cell lines (instant claims 1 and 2; see Tables 1 and 2, page 2156, all of paragraph 5, and page 2157, all of paragraphs 1 and 2). Kallioniemi teach that copy number increases of the 17q22-24 region were found in 18% of primary breast tumors and 67% of breast cancer cell lines examined (see Tables 1 and 2 and page 2159, paragraph 2, lines 5 and 6 of Kallioniemi). This above method taught by Kallioniemi involves comparative genomic hybridization in which the relative intensity of a fluorescent signal from a test chromosome (from tumor cells for example) hybridized with a labeled probe is compared to the intensity of a fluorescent signal from a control chromosome hybridized with the same probe that emits a different fluorescent color (instant claims 1-3, 39-44 and 48-53; see page 2156, paragraph 2, lines 3-8 of Kallioniemi). Kallioniemi teaches that the probe/chromosome hybridizations of the above method were analyzed using a digital image analysis system that was based on either a Nikon SA or Zeiss Axioplan microscope equipped with a cooled

charge-coupled device camera and a filter system consisting of a triple-band-pass beam splitter and emission filters and therefore the data was stored in an electronic video format (instant claim 3; see Figure 1 and page 2157, paragraph 3, lines 1-6 of Kallioniemi). Kallioniemi further teaches that three-color images derived from the above method were processed with a Sun IPX workstation using Scil-Image software for pseudocolor display and therefore the data was analyzed via video display and compared and compiled at a location where the data was transmitted (instant claim 3; page 2157, paragraph 3, lines 11-14 of Kallioniemi).

Response to Arguments

9. The response traverses this rejection. The response asserts that Kallioniemi et al. provides no specific teaching that a WIP1 gene or a WIP1 gene having a nucleotide sequence homology of at least 70% sequence identity to SEQ ID NO:1 or 3 has any associated with breast cancer but merely teaches that chromosomal regions including 17q22-q24 are amplified in certain breast cancer cell lines and primary tumors (page 13). The response further asserts that the disclosure date of Wu et al., 07/01/2001, is later than the date of the instant application's priority, 02/14/2001, and therefore is not proper prior art and should not be used to supplement the teachings of Kallioniemi et al. This argument has been thoroughly reviewed but was not found persuasive. The examiner notes MPEP 2112, section 2:

There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also Toro Co. v. Deere & Co., 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); Abbott Labs v. Geneva Pharms., Inc., 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1310 (Fed.Cir.1999) ("If a product that is offered for sale inherently possesses each of the limitations of the claims, then the invention is on sale, whether or not the parties to the transaction recognize that the product possesses the claimed characteristics."); Atlas Powder Co. v. Ireco, Inc., 190 F.3d 1342, 1348-49 (Fed. Cir. 1999) ("Because sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention.... An inherent structure, composition, or function is not necessarily known.")>; SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005) (holding that a prior art patent to an anhydrous form of a compound "inherently" anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the anhydrous compound "inherently results in at

least trace amounts of" the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate).

Therefore, the examiner maintains that Wu et al. is properly used in this rejection to define that the human WIP1 gene is located in the 17q22-23 region of chromosome 17 which was found amplified in breast tumors by Kallioniemi. The examiner notes that according to the DB SNP database, 10 polymorphisms have been found in the human Wip1 gene including the genomic region (see NCBI, DP SNP report). Assuming that the Wip1 gene is at least as large as SEQ ID NO:3, the mRNA transcript which is 2.9 kb, the frequency of polymorphisms in Wip1 would indicate that the Wip1 gene in the chromosome 17 region found amplified by Kallioniemi was at least 99.7% identical to the sequences of SEQ ID NO: 1 or 3. In addition, it is noted that the specification defines "percentage of sequence identity" as being calculated over a comparison window with no definition of the sequences within the claimed sequences that can be used for the comparison window (page 20). Therefore, it is highly likely that the Wip1 gene in the chromosome 17 region found amplified by Kallioniemi would contain regions of sequence in comparison windows that are identical to that of SEQ ID NO:1 or 3. Therefore, the examiner maintains that Kallioniemi as defined by Wu teach a method of detecting and measuring DNA sequence copy number increases for the 17q22-24 region, which contains the human WIP1 gene of at least 99.7% identity and likely 100% identity in certain regions to SEQ ID NO:1 and 3, in several human primary breast tumors and breast cancer cell lines.

For these reasons and the reasons already made of record, the rejection is maintained.

10. Claims 1-3 and 39-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Lavi (herein referred to as Lavi, WO 97/10796, 03/1997), as defined by Fiscella et al. (herein referred to as Fiscella, 1997, PNAS USA, Vol. 94, pages 6048-6053).

Regarding instant claim 1, it is noted that the examiner has given "gene copy number' the broad interpretation of the relative number of copies of the DNA sequence that encodes the products of the gene or any RNA expression products encoded by the gene.

Lavi teaches a method of detecting cancer in a patient by detecting alterations in gene activity of the protein phosphatase 2Calpha (PP2Calpha) gene, a member of the same family of phosphatases as WIP1 (broadly interpreted as a WIP1 homolog as broadly defined by the specification on pages 21 and 22), and genetic polymorphisms thereof in a specimen isolated from the patient wherein the gene activity of the patient is compared to normal controls (instant claim 1; see page 9, lines 24-30 of Lavi). Fiscella teaches that PP2Calpha which has regions of >70% sequence identity to human WIP1 (see page 6050, column 1, para 1, lines 11-15 of Fiscella). Lavi teaches that the genetic polymorphisms detected by the above method encompass variations that produce *increased levels* of gene product (instant claim 1; see page 10, lines 8-12 of Lavi). Lavi teaches that samples used with the above method can be biopsied material from suspected precancerous lesions of any tissue or bodily fluid which can be assayed

for PP2Calpha activity or gene product (instant claim 1; see page 11, lines 14-19 of Lavi). An example of the above method taught by Lavi is in Example 5 of Lavi where the expression level of PP2Calpha RNA is measured in colorectal cancer patient tissues in comparison to normal colon tissues (instant claims 1 and 2; see all of Example 5 on pages 45 and 46 of Lavi). The data from Example 5 of Lavi was physically transferred to paper as shown in Figure 7 of Lavi and can be compared and compiled at the location where the data is transmitted (instant claim 3).

Response to Arguments

11. The response traverses this rejection. The response asserts that Lavi neither teaches nor suggests a method of diagnosing a precancerous lesion or a cancer by detecting and measuring the gene copy number of a WIP1 gene or a method of diagnosing a precancerous lesion or a cancer by detecting and measuring the gene copy number of a WIP1 gene having a sequence homology of at least 70% sequence identity to SEQ ID NO:1 or 3. This argument has been thoroughly reviewed but was not found persuasive. It is noted that the specification defines "percentage of sequence identity" as being calculated over a comparison window with no definition of the sequences within the claimed sequences that can be used for the comparison window (page 20). As noted above in para 10, Fiscella teaches that the PP2Calpha gene has regions of >70% sequence identity to human WIP1 and PP2Calpha is highly likely to have regions of 100% identity in certain comparison windows. Therefore, PP2Calpha,

the gene detected in the method of detecting cancer taught by Lavi, is a sequence having at least 70% identity to SEQ ID NO:1 or 3 as defined by "percentage of sequence identity" in the instant specification.

For these reasons and the reasons already made of record, the rejection is maintained.

Conclusion

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas O'Farrell whose telephone number is (571) 272-8782. The examiner can normally be reached Monday-Friday from 8:30 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Thomas O'Farrell
Examiner
Art Unit 1634

Thomas O'Farrell
2/6/06

Jehanne Sitton
JEHANNE SITTON
PRIMARY EXAMINER
2/6/06